

# Operative Management of Impending Pathological Fractures: A Critical Analysis of Therapy

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**Background:** Evident and impending pathological fractures should be stabilised operatively because patients are in serious pain and debilitated for their remaining life span.

**Methods:** We evaluated survival and functional results after operative therapy. A retrospective study was conducted concerning 116 patients with 152 impending pathological fractures.

**Results:** Of all operated patients, postoperatively 79% regained walking capacity and 60% required no or only occasional analgesic drugs. Patients operated on for impending pathological fractures showed better functional results, as well as those operated with the additional use of polymethylmethacrylate (PMMA). Prophylactic use of antibiotics reduced the number of infectious complications significantly. The median survival after operative therapy was 15 months.

**Conclusions:** We conclude that impending pathological fractures should be operatively stabilised, if possible, with the additional use of PMMA because of better functional results.

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**KEY WORDS:** operative therapy; bone metastasis; functional results; PMMA; concomitant metastasis; radiotherapy

## INTRODUCTION

Metastatic bone disease is the most frequent neoplasm of the bone. Based on postmortem studies, it is estimated that 80–90% of all patients suffering from disseminated malignant disease will eventually demonstrate bone metastasis. Approximately 10% of the patients with skeletal metastasis will develop a pathological fracture, although reported data vary from 2% to 30% [1–5]. Vertebrae, femur, pelvis, and humerus are frequently affected because locations with the greatest biomechanical load are most at risk for fracturing.

Breast cancer accounts for 50% of all pathological fractures [5]. Other “bone-seeking tumors” are renal cell carcinoma and lung, prostate, and thyroid cancer. Intensification of palliative treatment has prolonged survival rates of patients suffering from several of these primary

tumors during the last decennia. As a consequence the surgeon is more frequently challenged with treatment of patients with pathological fractures. Conservative treatment is generally not optional, because it would mean a long hospital stay with inconveniences and complications. Therefore, tumor-specific internal fixation or prosthetic implants must be used with the additional use of polymethylmethacrylate (PMMA). This has the advantage of unprotected weight bearing, which is of crucial importance for these patients.

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**TABLE I. Distribution of Primary Tumors of Pathological Fractures**

Diagnosis	Number of patients	Percentage
breast cancer	49	42
renal cell carcinoma	14	12
lung cancer	10	9
prostate cancer	10	9
thyroid cancer	5	4
unknown primary	5	4
laryngeal cancer	4	3
malignant melanoma	2	2
malignant Schwannoma	2	2
others	15	13
total	116	100

In this study, an analysis is made of patients treated with internal fixation in combination with PMMA, additional radiotherapy, and antibiotic prophylaxis.

### MATERIALS AND METHODS

A retrospective study of patients with (impending) pathological fractures of the long bones, treated in the period 1983–1993, was performed. It concerned 116 patients with a total of 152 fractures. The population consisted of 71 females and 45 men, with a median age of 62 years (range 6–85 years).

Breast cancer was the most frequent primary tumor (42%), followed by renal cell carcinoma (12%), lung cancer (9%), prostate cancer (9%), and thyroid cancer (4%); Table I. Of the fractures, 56% were evident ( $n = 85$ ), and 44% were impending pathological fractures ( $n = 67$ ). Evident fractures occurred spontaneously in 61%, due to an inadequate trauma in 8%, to an adequate trauma in 10%, and unknown in 21%.

For 59%, this was the first pathological fracture; 23% of the patients had their second and 10% their third pathological fracture. One patient even had sustained his tenth fracture.

All patients were operated in case of an evident pathological fracture. In case of an impending fracture, patients were operated if the metastatic lesion was a lytic lesion, measuring  $>2.5$  cm (in the femur), showed  $>50\%$  cortex destruction of any long bone, or caused persistent pain not responding to radiotherapy. Patients were excluded for operative management if their general condition did not allow for general anaesthesia. Life expectancy was no criterion with the exception of patients who were expected to die within a few weeks.

The most frequent locations were the femur (59%, of which 83% were in the proximal part), the humerus (20%), the spine (8%), and the pelvis (7%).

A total of 110/152 fractures were treated operatively (72%), 27 with irradiation (18%), and 15 were treated conservatively (10%). Operative management consisted

in 51% of plate-osteosynthesis, in 23% of intramedullary nailing, in 14% of prosthetic implants, and in 6% of (partial) resection.

We studied the pre- and postoperative level of mobility, the postoperative use of analgesic drugs, whether or not PMMA and antibiotics were used during the operation, and the effect of additional radiotherapy. Furthermore, we looked at the presence of concomitant metastatic lesions on admission (other organs than the skeleton) and at survival after treatment.

## RESULTS

### Mobility

Detailed information as to the level of pre- and postoperative mobility was available for only 60 patients with fractures of the femur. We found that 63% of the patients were completely mobile before the fracture occurred. Mobility was suboptimal in 32% (patients used a crutch or stick), one patient was in a wheelchair, and two patients were already bedridden. The maximum level of postoperative mobility was optimal in 42% of the patients, suboptimal in 37%, wheelchair-bound in 10%, and bedridden in 11%.

Twenty-six of 60 patients showed a decreased level of mobility postoperatively (43%). Twenty-nine patients were equally mobile (48%), and five patients were more mobile than before the operation (9%). None of the patients with impending fractures and a (sub)optimal mobility showed a decreased level of mobility postoperatively, in contrast to 31% of the patients with evident fractures. These differences are statistically significant (Fisher's exact test  $P < 0.01$ ).

In 55% of the operations, PMMA was applied. Of the PMMA-treated patients, 70% were completely mobile, 27% had a suboptimal mobility, and one patient was already bedridden before the (impending) fracture occurred. Postoperatively, only 43% of the patients had optimal mobility, 47% suboptimal, two patients were confined to a wheelchair (7%), and one patient was bedridden (3%).

Of the patients who were treated without PMMA, 60% were preoperatively completely mobile, 32% had a suboptimal mobility, one patient was in a wheelchair, and one was bedridden. After operative therapy, 40% had an optimal mobility, 28% suboptimal, 12% were bound to a wheelchair, and 20% were bedridden. The differences between the two patient groups were not statistically significant (Fisher's exact test  $P = 0.16$ ).

### Relief of Pain

Nearly all patients preoperatively had pain and used a nonsteroidal antiinflammatory drug or a narcotic drug occasionally. After operative management, 29% of the patients had total relief of pain, 45% experienced partial

relief, and 16% had no benefit. In the postoperative period, 49% of the patients did not need any drug at all, 11% needed a nonsteroidal antiinflammatory drug, 22% a narcotic drug, and 8% needed both types of analgesics. Statistical analysis showed no significant differences between the two patient groups for pain relief (Fisher's exact test  $P = 0.23$ ), nor for the use of analgesic drugs (Fisher's exact test  $P = 0.1$ ).

### Complications

Most complications were infectious (21% of all complications) and haematologic (also 21%) in nature. Of all the operations, 20% had a bone-related complication and four patients died within 1 week after the operation. Bone-related complications included failure of the osteosynthetic device or prosthetic implant as well as progression or re-occurrence of the disease within the operative field.

Bone-related complications were independent of the use of PMMA. Twenty percent of PMMA-treated patients and 20% of those treated without additional PMMA suffered from one or more bone-related complications. In the nonirradiated group, 21% had complications vs. 14% in the patients who had received additional radiotherapy. Although just a minority of our patients had been treated with additional radiotherapy (28%), the difference is remarkable but not statistically significant.

Sixty percent of the operations were performed with antibiotic prophylaxis. In this patient group, infectious complications occurred in 5%, in contrast to 24% in patients without antibiotic prophylaxis. This difference is statistically significant (Fisher's exact test  $P = 0.02$ ).

As to the type of fracture, out of 45 operations for impending pathological fractures, 20 were followed by one or more complications. Nine of those were bone-related complications (20% of the operations). Of the 65 operations for evident fractures, 34 were followed by one or more complications, of which nine were bone-related (14%).

### Survival

The median "fracture-free" interval, the length of time between diagnosing the primary tumor and the first pathological fracture, was 2.6 years (range 0.4–11.6 years). For patients with breast cancer, this was 3.7 years, with prostate cancer 3.9 years, renal cell carcinoma 1.8 years, and lung cancer 0.4 years.

The median survival after treatment of the first pathological fracture was 15 months, with a range of 1 day to 10 years. Patients suffering from breast cancer had the best prognosis with a median survival of 24 months. Survival rates of the four most frequent primary tumors are shown in Table II. The differences in survival are statistically significant (Log-rank test  $P = 0.02$  and the Wilcoxon test  $P < 0.01$ ).

**TABLE II. Median Survival in Months After First Pathological Fracture\***

Primary tumor	Number of patients	Survival	Range
breast cancer	49	24	0–118
renal cell carcinoma	14	17	0–24
prostate cancer	10	12	2–35
lung cancer	10	2	0–28
all	116	15	0–118

\*For the four most frequent primary tumors.

Concerning metastasis, 45% of the patients had no metastatic lesions outside the skeleton, 40% had proven lung- and/or skin metastasis (these were the most frequent locations), and 15% had metastasis at less frequent locations. The median survival in the first group of patients was 23 months, in the second 15 months, and in the latter 19 months. The differences were statistically not significant (Log-rank test  $P = 0.25$  and the Wilcoxon test  $P = 0.42$ ).

### DISCUSSION

Pathological fractures impair a patient's mobility considerably and often create therapy-resistant pain, especially fractures of the femur, which can seriously reduce the quality of life for the remaining life-span. It is of fundamental interest to recognize an impending pathological fracture in time so that operative management can take place before fracture occurs. Not only the operative procedure will be of less magnitude and less frequently complicated, but also the functional result for the patient will be better. The main goal of treatment of patients with pathological fractures is preserving or regaining mobility to an acceptable level or improving the possibilities for adequate nursing care. The result of operative management of pathological fractures of the femur on mobility proved very successful. Of all patients with an impending or evident pathological fracture of the femur, 79% regained full walking ability or just had to use a cane or crutches. Our results are comparable to those reported in recent literature [6–8].

Another goal in the management of pathological fractures is alleviation of pain. Due to operative therapy, significant pain relief was realized in 74% of the operated patients, which is in accordance with other studies [6,9]. Of all patients, 60% required no analgesic drugs at all or just used a nonsteroidal antiinflammatory drug occasionally. In our study, the additional use of PMMA had no significant beneficial effect on the amount of pain relief. However, Haberman found a statistically significant difference in pain relief of 97% with the use of PMMA, and 83% without PMMA [2,10].

In patients suffering from metastatic bone disease, other organ systems are frequently affected. Metastatic lesions in the lungs or liver are often diagnosed on ad-

mittance. In addition they commonly suffer from malnutrition, general muscle weakness, respiratory insufficiency, and hypercalcemia. These factors make patients in general more predisposed to various complications. An impaired host defence (whether or not due to chemotherapy) in combination with the osteosynthetic implant makes them more vulnerable to infections. In trying to minimize this risk, not only the surgeon's skill is more challenged, but also wound lavage, judicious haemostasis, and perioperative antibiotic prophylaxis are of utmost importance.

According to the literature, bone-related complications are the most likely to occur, although the reported data vary widely. Some studies found fixation failures in 4.7–9.2% of all operations; others found 19% osteosynthesis-related complications and 19% tumor-related complications [6,8,11–13]. We found bone-related complications after 20% of all operations ( $n = 110$ ) of which 11% was osteosynthesis- and 10% tumor-related.

We did not find an increased complication rate after the additional use of PMMA. There are not many studies that could find a significant difference in this respect [2]. Reported side effects of PMMA are cardiovascular depression during insertion in the medullary space and non-union [14,15]. In our study, cardiovascular depression was seen in none of the 58 operations in which PMMA was used.

Intramedullary fixation stabilises the entire length of the long bone and is a much easier and less time-consuming procedure, contrasted to plate osteosynthesis. Therefore, some authors report that intramedullary fixation has less bone-related complications. We found bone-related complications after 16% of all intramedullary fixations ( $n = 25$ ) and after 25% of all plate osteosyntheses ( $n = 56$ ).

Rigid fixation is one of the prerequisites of pain relief. In many fractures, unfortunately, bone destruction is so extensive that secure internal fixation is impossible by conventional methods. The additional use of acrylic cement (PMMA) has proven to be a beneficial and safe method to accomplish secure fixation [15,16–19]. In our PMMA-treated group, 90% of the patients regained full walking ability or had to use an aid. In the group treated without PMMA, this was 68%. This difference is not statistically significant (Fisher's exact test  $P = 0.09$ ). The number of patients with preoperative full walking ability is larger in the PMMA-treated group, which might have been a confounding factor. These results more or less confirm the data found in the literature. Bouma found a completely regained walking ability within 1 week of 43.5% in the group without PMMA and 76.9% in the group with PMMA used [20]. Habermann showed that 90–95% of the PMMA-treated patients (who were ambulatory preoperatively) regained walking ability, in contrast to 75% when PMMA was not used [2,10]. This

difference suggests a more adequate stabilisation of the fracture when PMMA was used. A contributing factor could be thermal necrosis of tumorous tissue during polymerisation of the methylmethacrylate, which theoretically can prohibit progressive destruction.

We found a total infection rate of 5% in patients who were treated with antibiotic prophylaxis, and 4% deep wound infections or sepsis. The importance of perioperatively administered antibiotics is expressed by the fact that 24% of the operations without antibiotics was followed by an infectious complication (Fisher's exact test  $P = 0.02$ ).

Radiotherapy is believed to play a major adjunctive role in the management of metastatic bone disease [21]. It will diminish the risk for soft tissue seeding and local recurrence [22].

In our study, only a minority of patients was treated with additional radiotherapy, but a striking difference was seen with patients treated without postoperative irradiation. We found 14% bone-related complications in patients who had additional radiotherapy, in contrast to 21% in patients who did not. These differences are statistically not significant, but it seems that postoperative radiotherapy impaired local recurrence and implant failure rates in our patients. Looking at the effect on pain relief, we see that there is a striking similarity between both groups. No statistically significant difference was found for pain relief, nor for use of analgesic drugs.

Metastatic lesions of long bones ideally should be fixated internally before fracture occurs. The criteria for impending fractures consist of both radiological and clinical components. These criteria have been the ground for discussion for many years [3,23].

We prefer prophylactic fixation because the patient is saved from the trauma of a pathological fracture, the operative procedure is of much less magnitude, has less complications, and less impact on limb function. We found that 44% of the operations on impending pathological fractures were followed by one or more complications, and 52% in cases of an evident pathological fracture. Although the total number of complications is higher in the group with evident fractures, the number of bone-related complications is higher in the impending group. A possible explanation might be a more aggressive management of evident pathological fractures. If this were the case, it also would be expressed in the postoperative level of mobility. But patients operated on for an evident pathological fracture more often had a decreased level of mobility. The data confirm that prophylactic fixation of an impending fracture has better functional results than internal fixation of an evident pathological fracture.

According to the literature, the mean survival after treatment of a pathological fracture varies from 5.0 months to 10.2 months [6,7,9,12,24–26]. Our studied

population showed a median survival of 15 months (range 1 day to 10 years). It must be noted that this survival is measured from operative therapy of the patient's *first* pathological fracture. None of the studies specify how many fractures the patients already had in the past. Patients suffering from breast cancer had the best prognosis (24 months) and patients with lung cancer the worst (2 months) in concordance with the known survival rates of the primary tumors.

There seems to be no correlation between the disease-free interval (from diagnosing primary tumor until first metastasis) and survival after treatment. A significantly better survival is seen when patients only have metastasis in the skeleton in contrast to those with concomitant lung- or liver metastasis [14]. Of our patients, 45% had no detected metastasis at other locations on admission, and these patients had a median survival of 23 months. There was no statistically significant difference with the patients with lung and/or skin metastasis who had a median survival of 15 months. The prognosis for patients with a pathological fracture after operative therapy seems to be impaired by concomitant metastatic lesions and is mainly determined by the kind of primary tumor and effectiveness of chemo and hormonal therapy.

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